



A STUDY ON THE OUTCOME OF PATIENTS OF CEREBRAL VENOUS SINUS THROMBOSIS TREATED WITH LMWH AT THREE MONTHS

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ABSTRACT CVT is an important cause of stroke usually in young population and women of child bearing age. The clinical features include diffuse headache, elevated intracranial pressure as well as papilledema and at times motor deficit along with seizures. The treatment of CVT comprises of low molecular weight heparins (LMWH), antithrombotic therapy with unfractionated heparin, oral anticoagulants, local thrombolysis by selective sinus catheterisation, intravenous thrombolysis etc. **Material & Methods:** An observational longitudinal descriptive study of 50 clinicoradiologically diagnosed CVT patients presenting in a duration of 15 months was undertaken. **Results:** A total of 50 cases included all adults of which 78% were male, 48% belonged to the age group 31-40 years. A significant number of patients had no comorbidities. Headache was the most common symptom in both males and female (90%). 58% patients had convulsions; altered sensorium was seen in 40% and focal deficit in 36%. And altered sensorium at presentation related with poor outcome. Multiple sinus involvement was seen in 82% cases out of which superior sagittal sinus was involved in 65% and transverse sinus in 66%. Treatment with LMWH had significant impact on clinical outcome at 3 months follow up and delay in treatment had adverse effect on outcome. **Conclusion:** CVT is disease most common in age group 31-40 years with male preponderance. Headache was the most common symptom and altered sensorium at presentation related with poor outcome. Multiple sinus involvement was seen most commonly out of which superior sagittal sinus and transverse sinus involvement were very common. Treatment with LMWH had significant impact on clinical outcome

KEYWORDS : Cerebral venous sinus thrombosis, superior sagittal sinus, transverse sinus, low molecular weight heparins, Barthel scale.

INTRODUCTION

Cerebral venous sinus thrombosis (CVT) is a type of venous thromboembolism and is rare but important cause of stroke especially in young population^[1,2,3]. It is enormously diverse in its mode of onset, clinical presentation, imaging appearance as well as outcome. As a result it poses tremendous diagnostic and therapeutic challenge^[4].

Approximately 0.5-1% of all strokes is CVT; frequently affecting the younger population, especially women of child bearing age; due to pregnancy, puerperium and oral contraceptive use^[5]. Pangariya et al reported CVT to account for half of all the strokes occurring in the young and 40% of those in women, in India.

Identification of predisposing factors is normally possible in nearly 80% patients and include hereditary prothrombotic conditions like Factor V Leiden mutatio, deficiency of protein C and S and antithrombin III, in addition to prothrombin gene mutations. Acquired risk factors include trauma, puerperium, antiphospholipid syndrome, pregnancy, surgery, exogenous hormones, cancer etc.

Superior Sagittal sinus is most frequently involved (72%) resulting in diffuse headache, elevated intracranial pressure as well as papilledema and at times motor deficit along with seizures. CVT may also occur in lateral venous sinuses and deep cerebral venous system including straight sinus, vein of Galen and internal cerebral vein^[6].

In view of clinical diversity and dearth of large sufficiently designed clinical trials, the optimum treatment of CVT still remains indecisive. The treatment of CVT comprises of therapeutic choices of low molecular weight heparins (LMWH), antithrombotic therapy with unfractionated heparin, oral anticoagulants, local thrombolysis by selective sinus catheterisation, intravenous thrombolysis and a combination of anti coagulation and thrombolysis apart from symptomatic therapy. Due to ambiguity in outcomes most clinicians consider treating all CVT cases with dose-adjusted heparin irrespective of the cause, clinical status or CT appearance; and that local thrombolysis is reserved for more extensive disease and clinical worsening.

Timely diagnosis and apt therapy perhaps diminishes morbidity, mortality and may even be life saving^[7]. CVT has been observed to have an acute case fatality of <5% and recovery in about 80% of patients without sequels. Owing to the lack of data in Indian population, this observational longitudinal study aims to evaluate the

patients of CVT who have been treated with LMWH and study the clinical outcome.

MATERIAL AND METHODS:

It was an observational longitudinal descriptive study, performed in the Department of Medicine, Army Hospital (Research and Referral), New Delhi. Study Population included patients aged 18 years and above presenting in OPD or admitted with clinical and radiological diagnosis of cerebral sinus venous thrombosis and treated with LMWH. The study was undertaken for a duration of 15 months. The patients were treated with LMWH subcutaneously on weight based regimens in therapeutic doses over 5 days and were then overlapped with oral Vit K antagonists. all the patients enrolled for the study were followed up after 3 months and were assessed on disability questionnaire.

In the form of modified Ranking scale and Barthel scale, those who had mRS of 3 or more or BI of 60 or less had poor functional status (bad outcome) and those who had mRS of 2 or less or BI of 60 or more had good functional status (good outcome).

Statistical testing was conducted with SPSS 17.0. The comparison of normally distributed continuous variables between the groups was performed using Student's t test. Pearson correlation was used to assess relationships.

RESULT AND DISCUSSION:

Our present study included a total of 50 cases who fulfilled the inclusion criteria and were treated with LMWH were enrolled in the study.

Table – 1 Age- Wise Incidence

Age group (years)	Number of cases	Percentage
18-30	10	20
31-40	24	48
41-50	11	22
>50	5	10
Total	50	100
Mean +/- SD	37.42 +/- 9.93	

In our study a significant proportion of patients (68%) were below 40 years of age with a mean age being 37.4 years. Numerous studies from India have found the mean age of patients to range from 31.3-48.7 years^[8,9].

Majority of the cases (48%) belonged to the age group 31-40 years; followed by 22% patients in the age group of 41-50 years and 10% of patients above 50 years. *Coutinho et al* also found the highest CVT incidence in the age group 31-50 years.

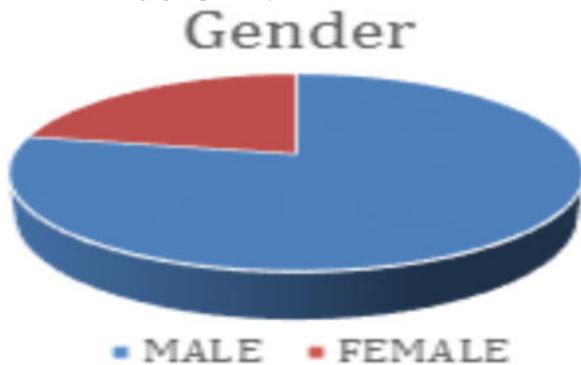


Figure 1: Gender-wise Distribution Of CVT Cases

Significant number of patients were males (78%) which is contradictory to the published literatures, as CVT is seen nearly 3 times more commonly in females^[10,11]. But *Parekh et al. and Narayan et al*^[8] found male predominance in their study.

Table – 2 Comorbidities In CVT Patients

Comorbidities	Number of cases	Percentage
None	12	24
Obesity	24	48
High Altitude	14	28
Alcoholism	11	22
Hypertension	7	14
Oral Contraceptive Pills	7	14
Smoking	5	10
Diabetes Mellitus type 2	2	4
APLA syndrome	1	2

A significant number of patients had no comorbidities. Among those with comorbidities, a significant difference was seen in the type of comorbidities gender-wise. In males alcoholism, hypertension and smoking was common whereas in women diabetes and OCP use was common.

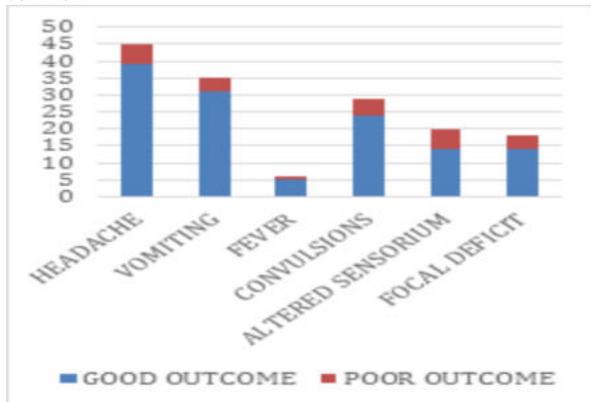


Figure 2: Symptoms And Outcomes In The CVT Patients

The current study found headache as the most common symptom in both males and female with 90% patients reporting it which is in concordance with the studies carried out by *Mosuhr et al* and *Gosk-Bierska et al*. 58% patients had convulsions, altered sensorium was seen in 40% and focal deficit in 36%. 35% patients reported vomiting and 6% had associated fever.

The current study found that those patients who had altered sensorium at the onset had consistent correlation with poor outcome compared to other symptoms, which is in agreement with the published studies^[12].

The present study found multiple sinus involvement in 82% cases out of which superior sagittal sinus was involved in 65%, transverse sinus in 66%, sigmoid sinus in 7% and straight sinus in 8%. *Ferro et al* reported SSS involvement in 62% cases^[12]. 71% cases of SSS

involvement followed by transverse and sigmoid sinus were reported by *Khealani BA et al*^[13].

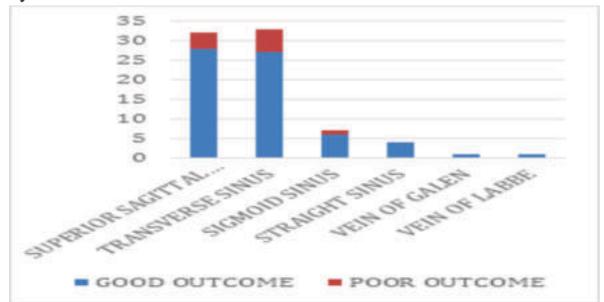


Figure 3: Cerebral Veins And Dural Sinuses Involved In CVT And Outcomes

In 30-40% cases more than one sinus is involved with or without cortical venous thrombosis^[14]. *Boussier et al* found that all 38 patients in their case series had TS involvement with SSS thrombosis which is close to our finding of 80% cases of multiple sinus involvement^[15]. None of the sinuses were significantly associated with poor prognosis.

Table – 3 Clinical Outcome After LMWH In CVT Patients By Barthel Index

Barthel Index	Good outcome (Mean+/-SD)	Poor outcome (Mean+/-SD)
At onset	80.35+/-12.22	66.43+/-11.44
After 3 months	98.14+/-3.94	77.14+/-10.35

In the present study, anticoagulants as the only means of treatment was the line of treatment in both males and females. *Ferro et al* reported that more than 80% patients administered with therapeutic doses of heparin for anticoagulation. *Coutinho JM et al* gave full dose heparin therapy to approximately 80% of both male and female patients. The above two studies attest the results in the present study and suggest that anticoagulants are the mainstay of therapy globally for CVT.

CONCLUSIONS:

Out of 50 enrolled patients in the study, a significant proportion of the patients were below 40 years of age with most prevalence observed between 31-40 years. Patients more 40 years age had poor prognosis. No significant difference was found between the age of the males and females.

A significant proportion of participants (78%) enrolled in the study were males. Males are more predisposed to have poor outcomes than females. In females 9% of CVT were puerperal but not associated with poor outcome.

High altitude, smoking, hypertension were common in males and OCP use and diabetes mellitus type 2 were common in females but none related to the clinical outcome.

Headache was commonest presentation (90%) followed by vomiting (70%), convulsions (58%), altered sensorium (40%) and altered sensorium at presentation related with poor outcome.

Multiple sinus involvement was seen in 82% cases out of which superior sagittal sinus was involved in 65% and transverse sinus in 66% of patients.

Treatment with LMWH had significant impact on clinical outcome at 3 months follow up and delay in treatment had adverse effect on outcome.

REFERENCES:

- [1] Saposnik G, Saposnik G, Barinagarrementeria F, Brown RD, Bushnell CD, Cucchiara B, Cushman M et al. Diagnosis and management of cerebral venous thrombosis: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2011 Apr 1;42(4): 1158-92.
- [2] Amoozegar F, Ronskley PE, Sauve R, Menon BK. Hormonal contraceptives and cerebral venous thrombosis risk: a systematic review and meta-analysis. *Frontiers in neurology*. 2015;6
- [3] Alvis-Miranda HR, Castellar-Leones SM, Alcalá-Cerra G, Moscote-Salazar LR. Cerebral sinus venous thrombosis. *Journal of neurosciences in rural practice*. 2013;4(4):427-38.
- [4] Boussier MG. Cerebral venous thrombosis: nothing, heparin or local thrombolysis. *Stroke*. 1999;30:481-3.
- [5] Allroggen H, Abbott RJ. Cerebral venous sinus thrombosis. *Postgraduate medical journal*. 2000 Jan 1;76(891):12-5.
- [6] Beamer HT, Bone I. Cerebral venous thrombosis: anticoagulants or thrombolytic

- therapy? *Journal of Neurology, Neurosurgery & Psychiatry*. 2000 Oct 1;69(4):427-30.
- [7] Kimber J. Cerebral venous sinus thrombosis. *QJM*. 2002 Mar 1;95(3): 137-42.
- [8] Ferro JM, Canhao P, Stam J, Bousser MG, Barinagarrementeria F, for the ISCVT investigators. Prognosis of cerebral vein and dural sinus thrombosis: results of the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT). *Stroke*. 2004;35:664-70.
- [9] Dash D, Prasad K, Joseph L. Cerebral venous thrombosis: An Indian perspective. *Neurology India*. 2015;63(3):318-328
- [10] Amoozegar F, Ronksley PE, Sauve R, Menon BK. Hormonal contraceptives and cerebral venous thrombosis risk: a systematic review and meta-analysis. *Frontiers in neurology*. 2015;6
- [11] Coutinho J. Cerebral venous thrombosis. *J Thromb Haemost*. 2015;13:S238-44.
- [12] Ferro JM, Canhao P, Stam J, Bousser MG, Barinagarrementeria F, for the ISCVT investigators. Prognosis of cerebral vein and dural sinus thrombosis: results of the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT). *Stroke*. 2004;35:664-70.
- [13] Khealani BA, Wasay M, Saadah M, Sultana E, Mustafa S, Khan FS, Kamal AK. Cerebral venous thrombosis a descriptive multicenter study of patients in Pakistan and Middle East. *Stroke*. 2008 Oct 1;39(10):2707-11.
- [14] Mehta SR, Muthukrishnan J, Varadarajulu R, Gupta A. Cerebral venous A great masquerader. *Medical Journal Armed Forces India*. 2004 Jul 1;60(3):299-301.
- [15] Shariff EM, Alhameed M. Multiple cranial neuropathies in cerebral venous sinus thrombosis. *Oxford Medical Case Reports*. 2014 May 1;2014(2):21-3.